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Estimating morbidity due to stroke in Nigeria: a systematic review and meta-analysis

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ABSTRACT

Background: The response to stroke in Nigeria is impaired by inadequate epidemiologic information. We sought to collate available evidence and estimate the incidence of stroke and prevalence of stroke survivors in Nigeria.

Methods: Using random effects meta-analysis, we pooled nationwide and regional incidence and prevalence of stroke from the estimates reported in each study.

Results: Eleven studies met our selection criteria. The pooled crude incidence of stroke in Nigeria was 26.0 (12.8-39.0) /100,000 person-years, with this higher among men at 34.1 (9.7-58.4) /100,000, compared to women at 21.2 (7.4-35.0) /100,000. The pooled crude prevalence of stroke survivors in Nigeria was 6.7 (5.8-7.7) /1000 population, with this also higher among men at 6.4 (5.1-7.6) /1000, compared to women at 4.4 (3.4-5.5) /1000. In the period 2000-2009, the incidence of stroke in Nigeria was 24.3 (95% CI: 11.9-36.8) per 100,000, with this increasing to 27.4 (95% CI: 2.2-52.7) per 100,000 from 2010 upwards. The prevalence of stroke survivors increased minimally from 6.0 (95% CI: 4.6-7.5) per 1,000 to 7.5 (95% CI: 5.8-9.1) per 1,000 over the same period. The prevalence of stroke survivors was highest in the South-south region at 13.4 (9.1-17.8) /100,000 and among rural dwellers at 10.8 (7.5-14.1) /100,000

Conclusion: Although study period does not appear to contribute substantially to variations in stroke morbidity in Nigeria, an increasing number of new cases compared to survivors may be due in part to limited door-door surveys, or possibly reflects an increasing mortality from stroke in the country.

HIGHLIGHTS

- There is very limited epidemiologic evidence on stroke morbidity in Nigeria.
- From crude estimates, new stroke cases appear to increase at relatively higher rates compared to stroke survivors.
- This possibly reflects inadequate door-to-door surveys, or an increasing mortality from stroke, both with implications for public health policy and planning.

INTRODUCTION

Stroke is a leading contributor to global disease morbidity and mortality (1). More than 6.5 million deaths and 113.2 million disability-adjusted life years (DALY) were attributable to stroke in 2013 (1, 2). Recent epidemiological trends revealed that global survivors for both ischemic and hemorrhagic stroke increased to 25.7 million in 2015, particularly in high-income countries (3). There are also new dimensions to these recent estimates. During the last decade, incidence rates and deaths from stroke in high-income countries have modestly diminished or plateaued resulting in about 42% reduction in overall stroke burden between 1970 and 2008 (4). In contrast, the burden of stroke has increased at an astonishingly fast rate in low- and middle-income countries (LMICs), with the steepest increase in stroke prevalence occurring in low-income countries of Africa, increasing by 6% annually (5). This evidence underscores a need for targeted effort by all stakeholder in these jurisdictions.

In Nigeria and across many African countries, the increasing burden of stroke has been attributed to epidemiologic and demographic transitions driven in part by both rural–urban drift and rapid economic development (4). The resulting population growth, ageing, physical inactivity and consumption of processed foods high in cholesterol and salt have contributed to increasing number of stroke cases seen in the last two decades (4). Simultaneously, inadequate neurological services and the high cost of health services remain serious challenges in many settings (6). In Nigeria particularly, the rising prevalence of cardiovascular risk factors, poor awareness of early stroke signs, high cost and poor uptake of computed tomography (CT) and magnetic resonance imaging (MRI) scans, have resulted in a rising 30-days stroke fatality (7).

Presently, there is insufficient information on the epidemiology of stroke in Nigeria (8, 9). Many stakeholders have advocated for accurate, up-to-date information on stroke incidence and survivorship to assist in identifying individuals, groups, or geographic areas that are at increased risk or poorer outcomes of stroke in the country. This study, therefore, aims to estimate the incidence of stroke and prevalence of stroke survivors in Nigeria to prompt improved policy response and public health intervention across at states and national levels.

METHODS

Search strategy

Database searches were conducted on 01 August 2018 and limited to studies published after 1 January 1990. We searched MEDLINE, EMBASE, Global Health, and Africa Journals Online (AJOL), for epidemiologic studies or reports on stroke in Nigeria. Search terms employed are shown in **Table 1**. Unpublished documents were sourced from Google Scholar and general Google searches. Titles and abstracts of studies were screened, and full-texts of relevant studies accessed. Reference lists of full-texts were further hand-searched for additional studies. We contacted authors of selected papers for any missing information.

Selection criteria

Studies that met inclusion were primarily population-based studies, community-based door-to-door surveys, or outpatient hospital surveys reporting on the prevalence or incidence of stroke in a Nigerian setting. We excluded studies on Nigerians in diaspora, case-reports, reviews, view-points or commentaries.

Case definitions

Stroke was defined according to standard WHO case definition: “rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting longer than 24 hours, unless interrupted by death, with no apparent cause other than that of vascular origin” (4, 10). We classified new cases of stroke as persons presenting with first ever stroke in a given period, while stroke survivors were the total number of people who have had stroke or living with its sequelae at a given time.

Data Extraction

Assessment of eligible studies was conducted separately by two reviewers (DA and AA), with a standardized eligibility guideline to ensure consistency. Any disagreement in study selection was resolved by consensus. Data on the location, study period, study design, study setting (urban or rural), sample size, diagnostic criteria and mean age of the population were extracted. These were matched with corresponding data on stroke cases (new or survivors), sample population (or person years of follow-up), and incidence or prevalence of stroke as reported in each study. For studies conducted on the same study site, population or cohort, the first published study was selected, and all additional data from the other studies were extracted and merged with data from the selected paper.

Quality Assessment

For each full text selected, we further screened for explicit description of methodology, case definitions of stroke, and generalizability of reported estimates to a larger population within the geo-political zone. For the quality grading, we adapted a previously used quality assessment criteria for studies examining the prevalence of chronic diseases (11-14). For each full-text manuscript selected, we screened for sampling strategy to identify if it was representative of a target subnational population, statistical methods (was it appropriate for the study outcome?),

and stroke case ascertainment (was it based on standard diagnostic criteria, unspecified clinical criteria, informant interviews, or not reported?). Studies were graded as *high* (4-5), *moderate* (2-3), or *low quality* (0-1) (see **Tables 2 and 3**, for details of all full-text manuscripts accessed and quality grading).

Data Analysis

A random effects meta-analysis, using the DerSimonian and Laird Method (15), was employed on the individual study estimates to generate national and sub-national summary estimates of incidence of stroke (expressed per 100000 person years (py)), or prevalence of survivors in Nigeria (expressed per 1000 population). Standard errors were determined from the reported crude estimates and population denominators, assuming a binominal (or Poisson) distribution. Heterogeneity between studies was assessed using I-squared (I^2) statistics, and subgroup analysis was conducted to detect causes of heterogeneity. Our approach to data analysis has been described in detail in previous studies (17, 18). All statistical analyses were conducted on STATA (Stata Corp V.14, Texas, USA). The study was conducted in strict compliance to the PRISMA guidelines (19).

RESULTS

Search results

Our searches identified 1199 potentially eligible studies (MEDLINE: n=522, EMBASE: n=650, Global Health: n=15, and AJOL: n=7). Five additional studies were identified through Google Scholar, and an examination of the reference lists of relevant studies. After duplicates have been removed, 602 titles were screened for relevance (i.e. any population-based or hospital-based studies on stroke in Nigeria). On applying the selection criteria, 533 studies were excluded. We then assessed 69 full-texts assessed following which another 58 studies were excluded. Eleven studies (6, 20-29) were finally selected for the review (**Figure 1**).

Study characteristics

Of the 11 retained studies, there were nine population-based surveys, while two were hospital-based. Four studies were retrieved from South-west Nigeria, three from the South-south, and two each from the North-central and South-east. There were no studies from the North-east and North-west. Six studies were conducted in urban settings, three in rural and two in semi-urban settings. Five studies were rated as high quality, while six were rated moderate. These 11 studies yielded 38 data points, 10 reporting incidence (which were mainly conducted in the South-west) and 25 pertaining to stroke survivors. Study period ranged from 1995 to 2016, with most studies conducted within a one-year period. The estimated person-years of follow-up from all studies was 1,242,137 and the total population covered among stroke survivors was 41,143. Mean age ranged from 26.9 to 58.2 years (**Table 3**). Heterogeneity was high across studies, with an I-squared (I^2) estimated at 100% and 97.7% for studies on new cases, and survivors, respectively ($p=0.001$ for both).

Pooled incidence of stroke in Nigeria

The estimated pooled crude incidence of stroke in Nigeria from all studies (1995-2016) was 26.0 (95% CI: 12.8-39.0) per 100,000 py (**Figure 2A, Table 4**). The incidence of stroke in men was higher at 34.1 (95% CI: 9.7-58.4) per 100,000 py, while women had an estimated incidence of 21.2 (95% CI: 7.4-35.0) per 100,000 py (**Table 4**). As all prevalence studies were reported mainly in the South-west, we did not conduct a sub-group analysis by geo-political zones. However, the incidence of stroke was highest among urban dwellers at 26.8 (95% CI: 75.1-80.5) per 100,000 py, while persons living in semi-urban settings (a mix of urban and rural environments) had a stroke incidence of 17.4 (95% CI: 15.2-19.6) per 100,000 py. There was no reported incidence in core rural settings (**Figure 2B, Table 4**). In the period 2000-2009, the incidence of stroke in Nigeria was 24.3 (95% CI: 11.9-36.8) per 100,000, with this increasing to 27.4 (95% CI: 2.2-52.7) per 100,000 in the period 2010 upwards (**Figure 2C, Table 4**).

Pooled prevalence of stroke survivors in Nigeria

As noted, there were more data points on stroke survivors, possibly reflecting the relative ease of identifying cases from community-based door-to-door surveys. The estimated pooled crude prevalence of stroke survivors in Nigeria was 6.7 (95% CI: 5.8-7.7) per 1,000 population (**Figure 3A, Table 4**). As observed for incident cases, the pooled crude prevalence of stroke survivors

was higher among men at 6.4 (95% CI: 5.1-7.6) per 1,000 compared to the pooled prevalence among women at 4.4 (95% CI: 3.4-5.5) per 1,000. Further sub-group analysis by geo-political zones in Nigeria showed that the South-south region had the higher prevalence of stroke survivors at 13.4 (95% CI: 9.1-17.8) per 1,000, followed by the South-east at 8.9 (95% CI: 3.4-14.5) per 1,000. The North-central and South-west zones had prevalence of 4.8 (95% CI: 2.7-6.9), and 2.9 (95% CI: 1.7-4.1) per 1,000, respectively. The prevalence of stroke survivors was higher in rural settings at 10.8 (95% CI: 7.5-14.1) per 1,000, while estimated prevalence in urban settings was 6.2 (95% CI: 4.6-7.9) per 1,000 (**Figure 3B, Table 4**). The prevalence of stroke survivors increased minimally from 6.0 (95% CI: 4.6-7.5) per 1,000 to 7.5 (95% CI: 5.8-9.1) per 1,000 over the period 2000-2009 and 2010 upwards (**Figure 3C, Table 4**).

DISCUSSION

The findings from this study revealed important information that mirrors the huge burden of stroke reported across sub-Saharan African countries (5). First, we found that the overall age-adjusted prevalence of stroke survivors in Nigeria was 674/100,000 population. This estimate is almost double the global estimate of 393.4/100,000 reported by Feign and colleagues in 2014, and also relatively higher than the ranges recorded in some LMICs (550/100,000) (30). Although the substantially higher estimate of stroke survivors may have been biased by underrepresentation of fatal cases, which have been noted in previous reports (7). Second, there was a significant variation in the prevalence of stroke survivors across regions and calendar years in Nigeria. Specifically, we found a higher prevalence trend among rural dwelling adults particularly in the South-south region compared to other regions or population groups in Nigeria. The evidence is also well situated in a previous survey of stroke prevalence, where a positive association was reported between cardiovascular diseases including stroke and environmental risks in the oil-rich rural South-south (Niger-Delta) region of Nigeria (31, 32). Hence, apart from lifestyle factors, this suggests increasing risks for stroke associated with exposure to environmental pollution in areas that host oil and gas production and refining operations in Nigeria. This finding is consistent with the estimates found in some low-income countries, in line with the convergence of increasing income levels, rural-to-urban transformation, and high industrial outputs towards cardio-vascular disease predictors (33).

When crude estimates were disaggregated by study period (*ie.* before and after year 2010), there were not so much difference in the incidence and prevalence rates, suggesting that year may not contribute substantially to variations in the morbidity of stroke in Nigeria (a fact further highlighted in an epidemiologic model we ran, see **supplementary material**). However, compared to a minimal increase observed among stroke survivors (6.0 to 7.5 per 100,000), crude incidence rates of stroke showed relatively higher increase, from 24.3 to 27.4 per 1000 before and after year 2010, respectively. This perhaps reflects an increasing mortality from stroke and/or limited capture of stroke survivors from household surveys, both with implications for public health policy and planning. Besides, the observed increase may be related to early stages of epidemiological transition Nigeria and indeed many LMICs are currently experiencing, characterized by higher rates of stroke and coronary deaths (5, 30). As noted, this has been linked to population-wide increased consumption of processed foods, higher salt intake, tobacco smoking, harmful use of alcohol, and sedentary lifestyles (34). Evidence of these changes in the country has come to the fore with a rising burden of cardiovascular outcomes including stroke mortality and morbidity as reported in this study and previously (4, 5, 7). The stroke rate found in this study is similar to the estimates from developing countries like Zimbabwe and Libya, however, this is lower in global age-adjusted annual incidence for LMICs, possibly reflecting poor data representation in many parts of the country (2). For instance, the age-adjusted incidence of stroke in countries like South Africa, Tanzania and Egypt ranges from 101 to 260 per 100,000 (30).

This portends huge burden to the overall health and economic development in Nigeria. This economic impact stems from increased out-of-pocket expenditure, loss of individual and family

productivity and reduced labour efficiency, thus culminating in underinvestment in other critical social infrastructure and GDP losses nationally. Developing a comprehensive nation-wide plan to address stroke and other NCDs, particularly through the promotion of healthy lifestyles among young adults and ensuring services are also available for rural dwellers, may provide a cost-effective approach to reducing this burden in the coming years (35-38).

This study has some important limitations to consider. First, our estimates and confidence intervals reflect wide uncertainties. This generally should guide the interpretation of our findings. The lack of data across many settings and calendar years is partly attributable, largely reflective of poor stroke infrastructure, especially stroke specialist registries, to track stroke cases particularly in rural areas. Second, in addition to lack of stroke registries, hospital-based data often may be inadequate to estimate incident cases due in part to unknown denominator or population at risk. Under-representation of cases could also be due to poor access to hospital services often related to distance and out-of-pocket costs for stroke services and care (39, 40). Third, although hospital-based studies are relatively preferred in the absence of stroke registry to investigate stroke incidence (34, 41), there were however insufficient information from most hospital-based studies to understand if these estimates were recurrent or first-ever strokes. Further, there were no studies from the North-east and North-west regions of Nigeria, and several important study characteristics including age- and sex-specific estimates were not always provided in studies. Thus, results arising from fewer data points may lean towards publication bias, underreporting of important metrics, and doubts on regional population representation.

However, this study also has important strengths. First, we applied a strict quality assessment based on methodological rigours in the selection of studies, ensuring only moderate to high quality studies were included in the analysis. This has important considerations in reducing bias from poorly designed studies, varying case definitions and poor population representation. Second, we applied a comprehensive systematic search of different databases to ensure the identification of relevant articles. Thus, this study has provided an updated information on the epidemiology of stroke in Nigeria, on which further research efforts can be established.

CONCLUSION

This study suggests incident cases and survivors from stroke may be increasing in Nigeria, and significantly vary across regions. The rise in stroke prevalence in the rural communities in Nigeria suggests that the risks for stroke may no longer be limited to urban dwellers. Public health awareness and other interventions for rural dwellers and other vulnerable population groups may be highly useful. It is hoped that the evidence provided in this study may inform relevant decisions, policy reforms and population-wide intervention towards reducing the burden of stroke across Nigeria.

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Authorship contributions: DA conceived and designed the study. DA and AA conducted literature searches for all databases. DA and ME wrote the first draft. DA and MOH conducted the analysis. DA, AA, MOH, ENN, NE, RGM, WA and IFA contributed to the final writing of the manuscript and checked for important intellectual content.

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FIGURE LEGENDS

FIGURE 1. Flow chart of selection of studies on stroke in Nigeria.

FIGURE 2. A. Pooled crude incidence of stroke in Nigeria, per 100,000 person years; **A.** Pooled crude incidence of stroke in Nigeria, per 100,000 person years (by study settings); **A.** Pooled crude incidence of stroke in Nigeria, per 100,000 person years (by study period).

FIGURE 3. A. Pooled crude prevalence of stroke survivors in Nigeria, per 1000 population (by geographic zones); **B.** Pooled crude prevalence of stroke survivors in Nigeria, per 1000 population (by study settings); **C.** Pooled crude prevalence of stroke survivors in Nigeria, per 1000 population (by study period).

FIGURE 1. Flow chart of selection of studies on stroke in Nigeria.

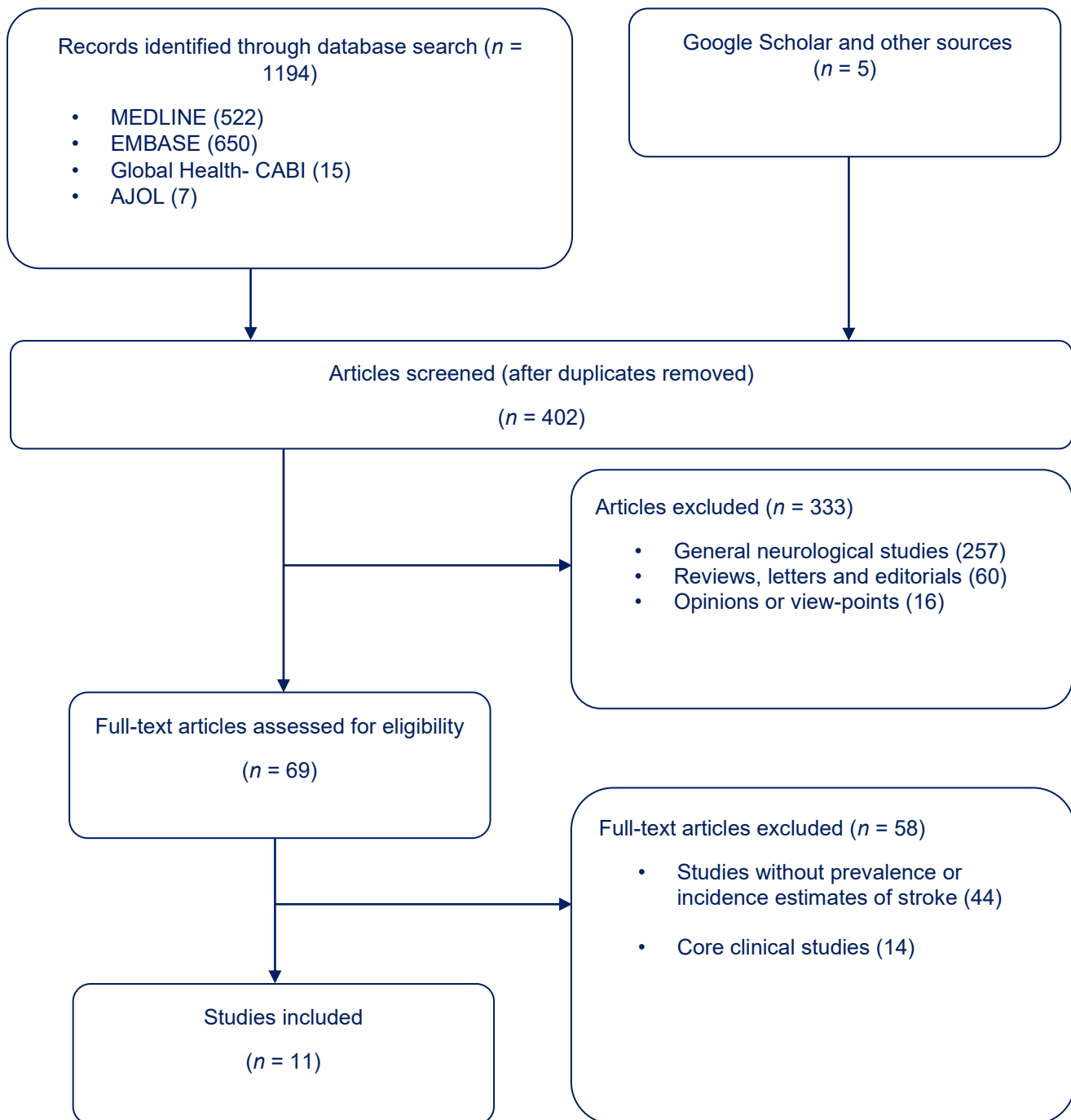
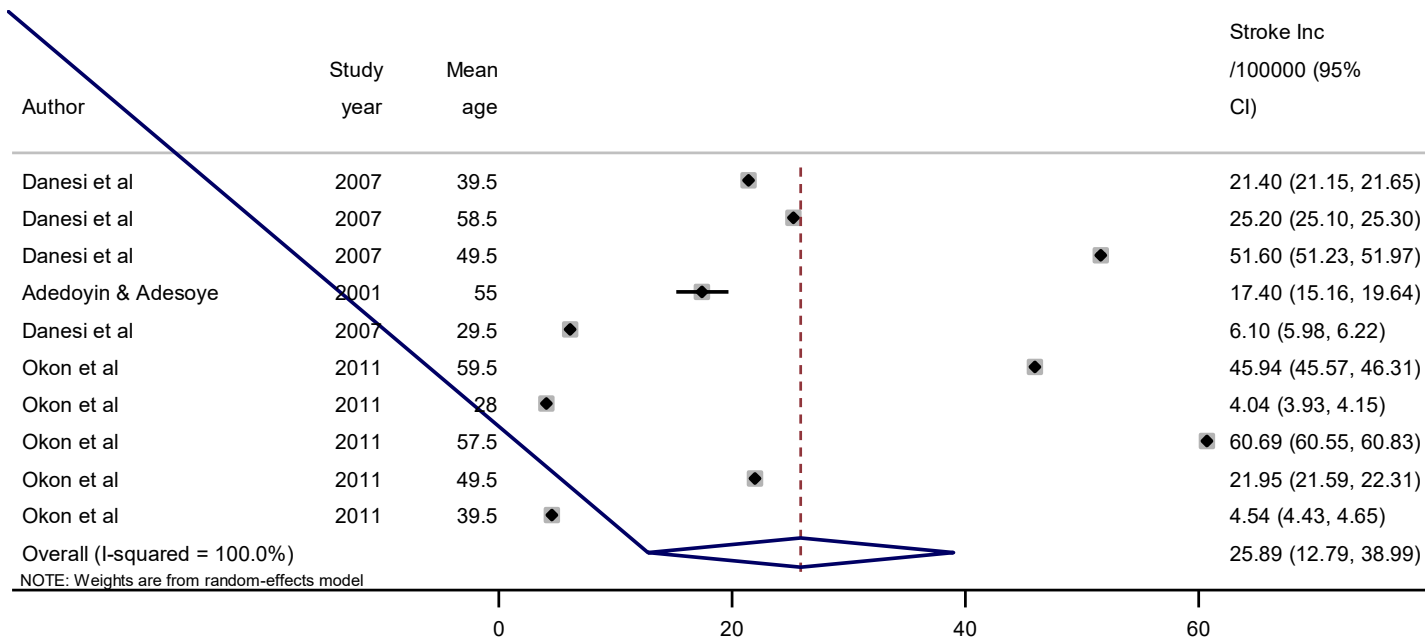
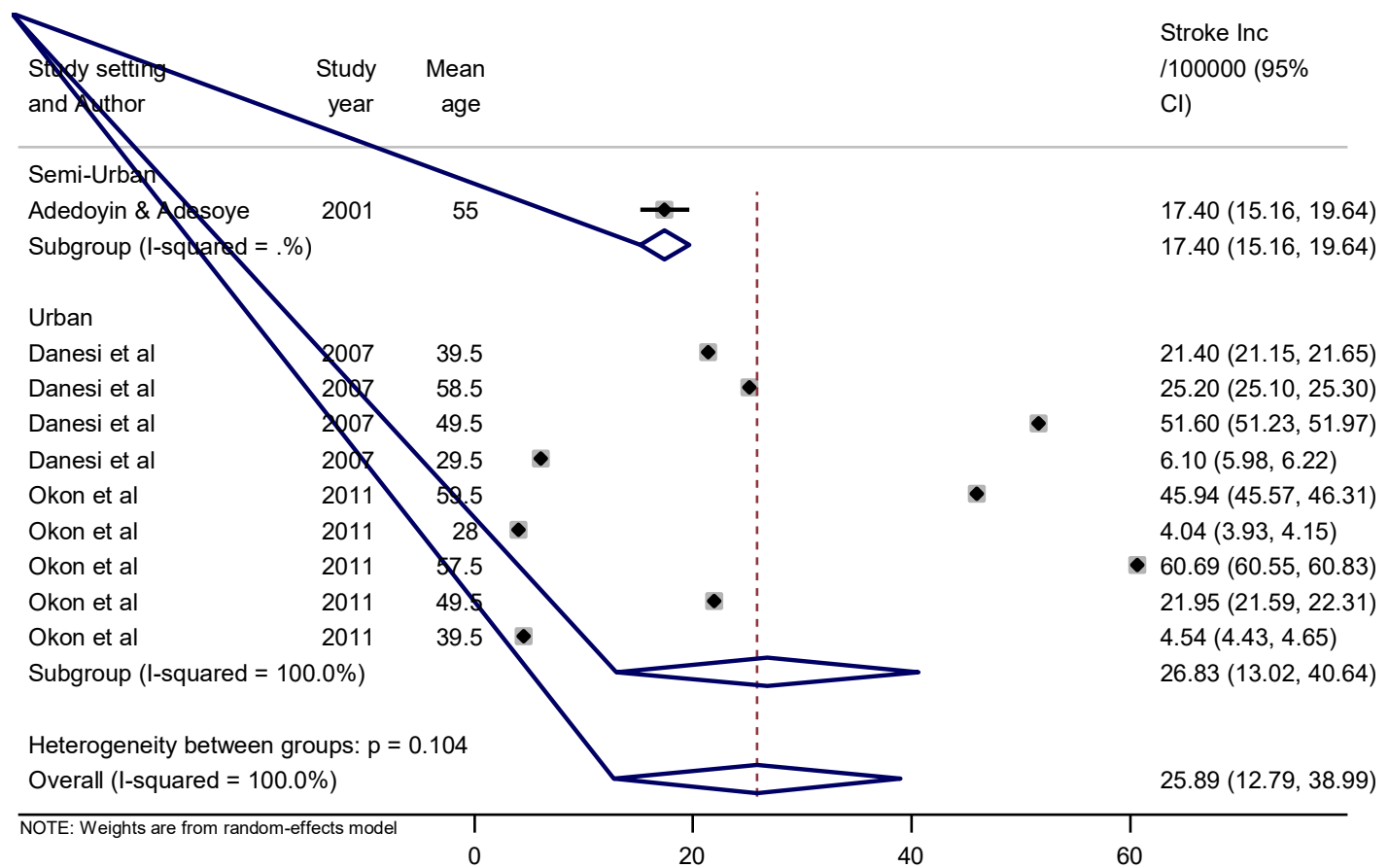


FIGURE 2. A. Pooled crude incidence of stroke in Nigeria, per 100,000 person years; **B.** Pooled crude incidence of stroke in Nigeria, per 100,000 person years (by study settings); **C.** Pooled crude incidence of stroke in Nigeria, per 100,000 person years (by study period).

A.



B.



C.

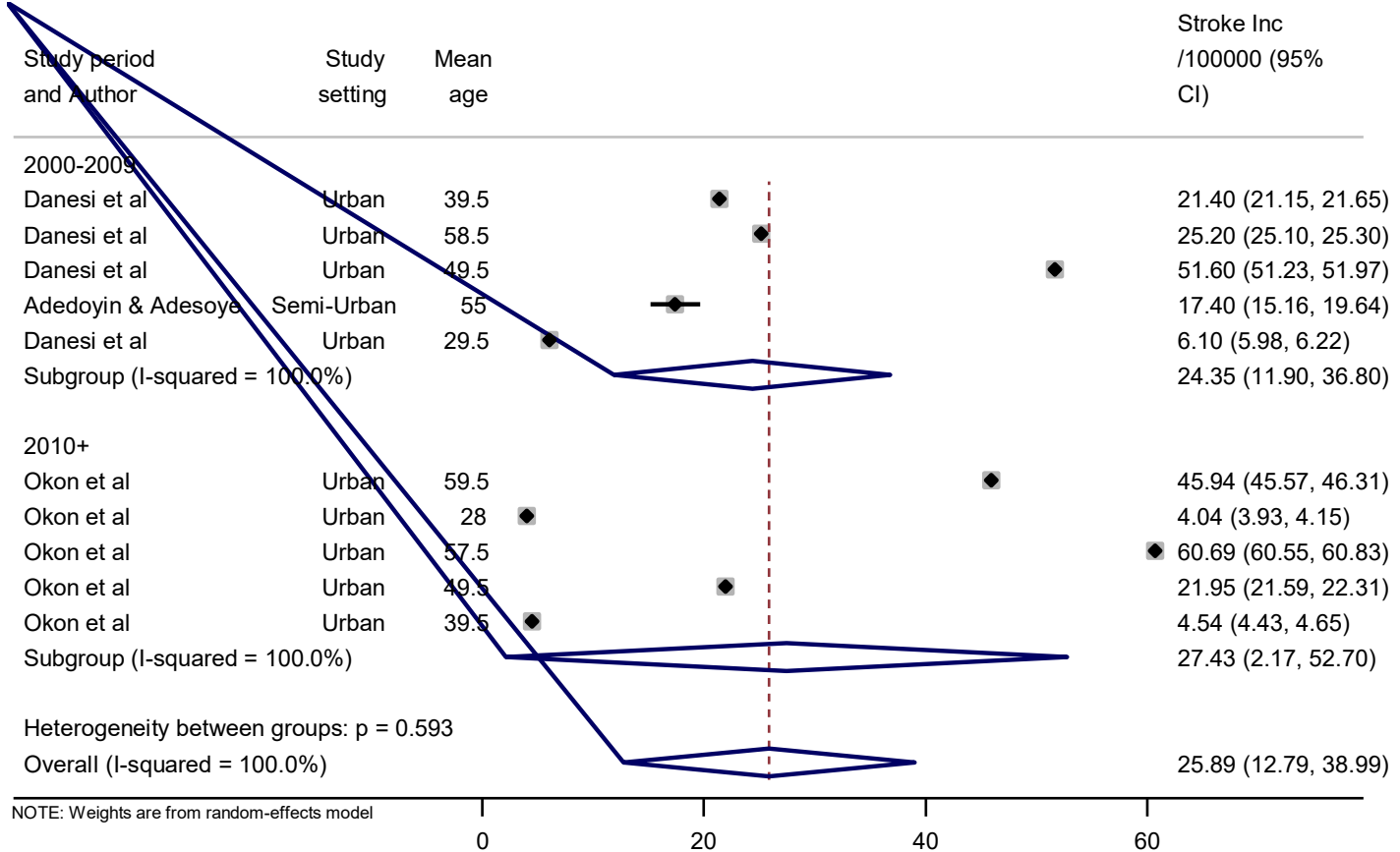
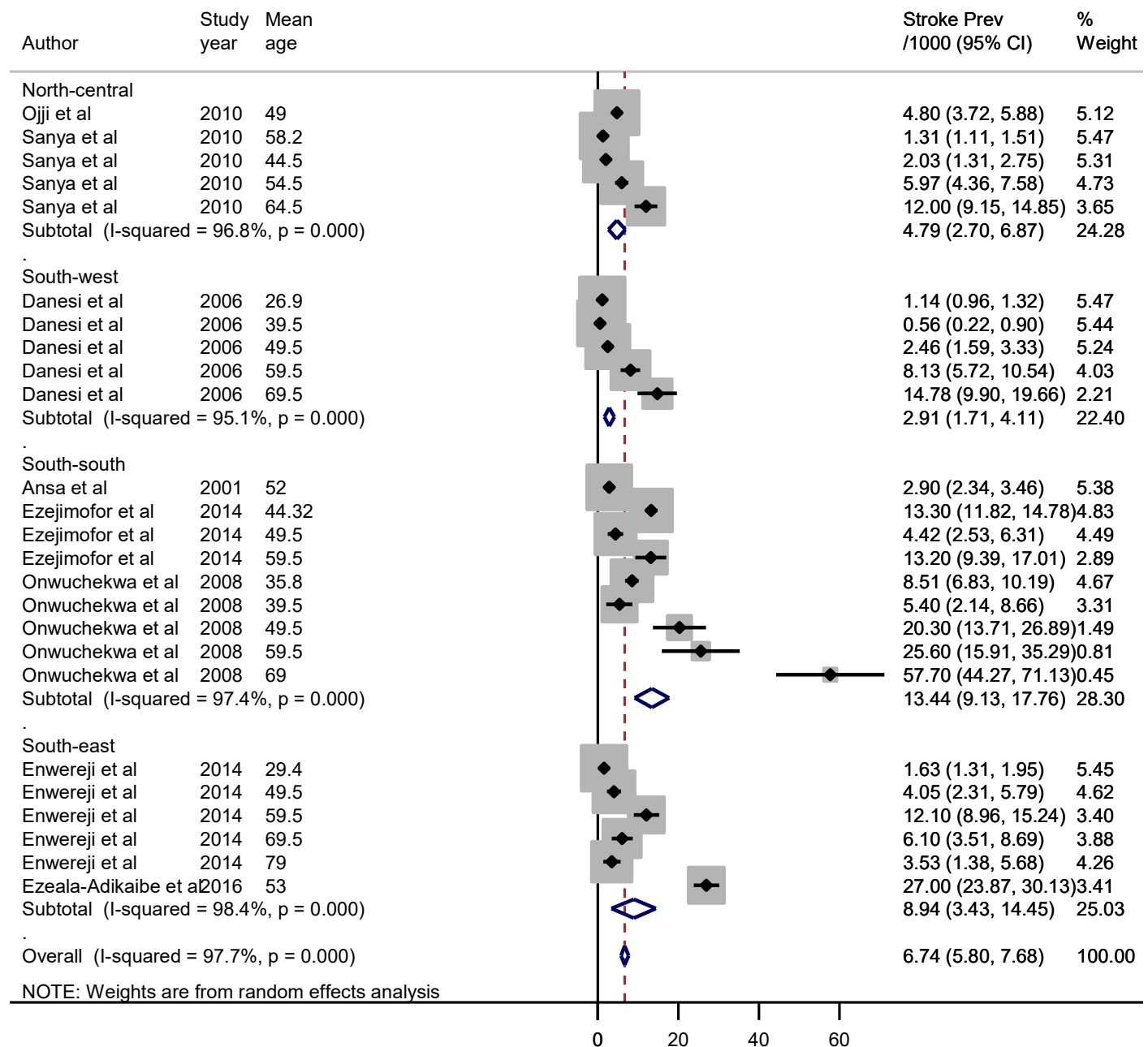
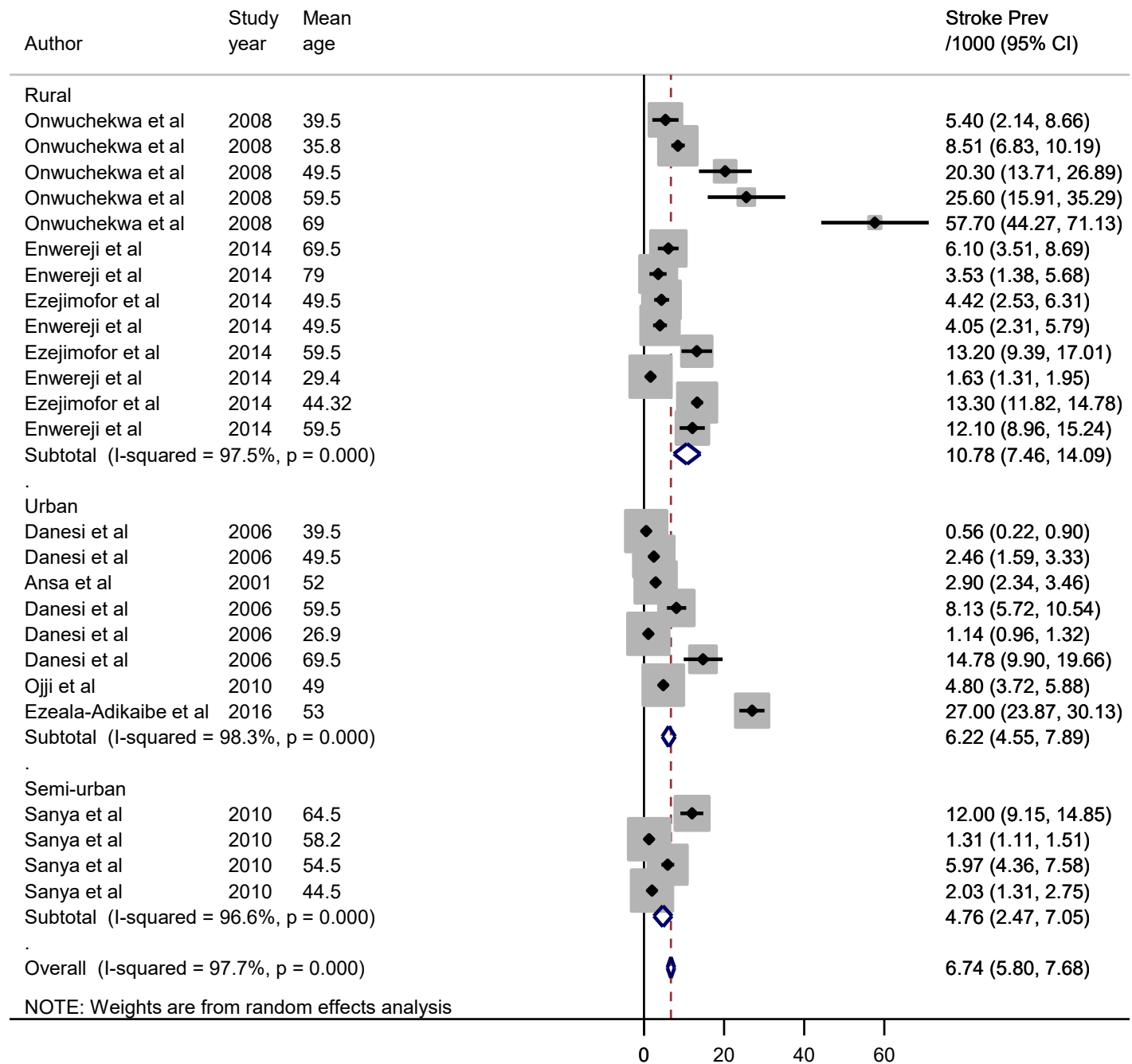


FIGURE 3. A. Pooled crude prevalence of stroke survivors in Nigeria, per 1000 population (by geographic zones); **B.** Pooled crude prevalence of stroke survivors in Nigeria, per 1000 population (by study settings); **C.** Pooled crude prevalence of stroke survivors in Nigeria, per 1000 population (by study period).

A.



B.



C.

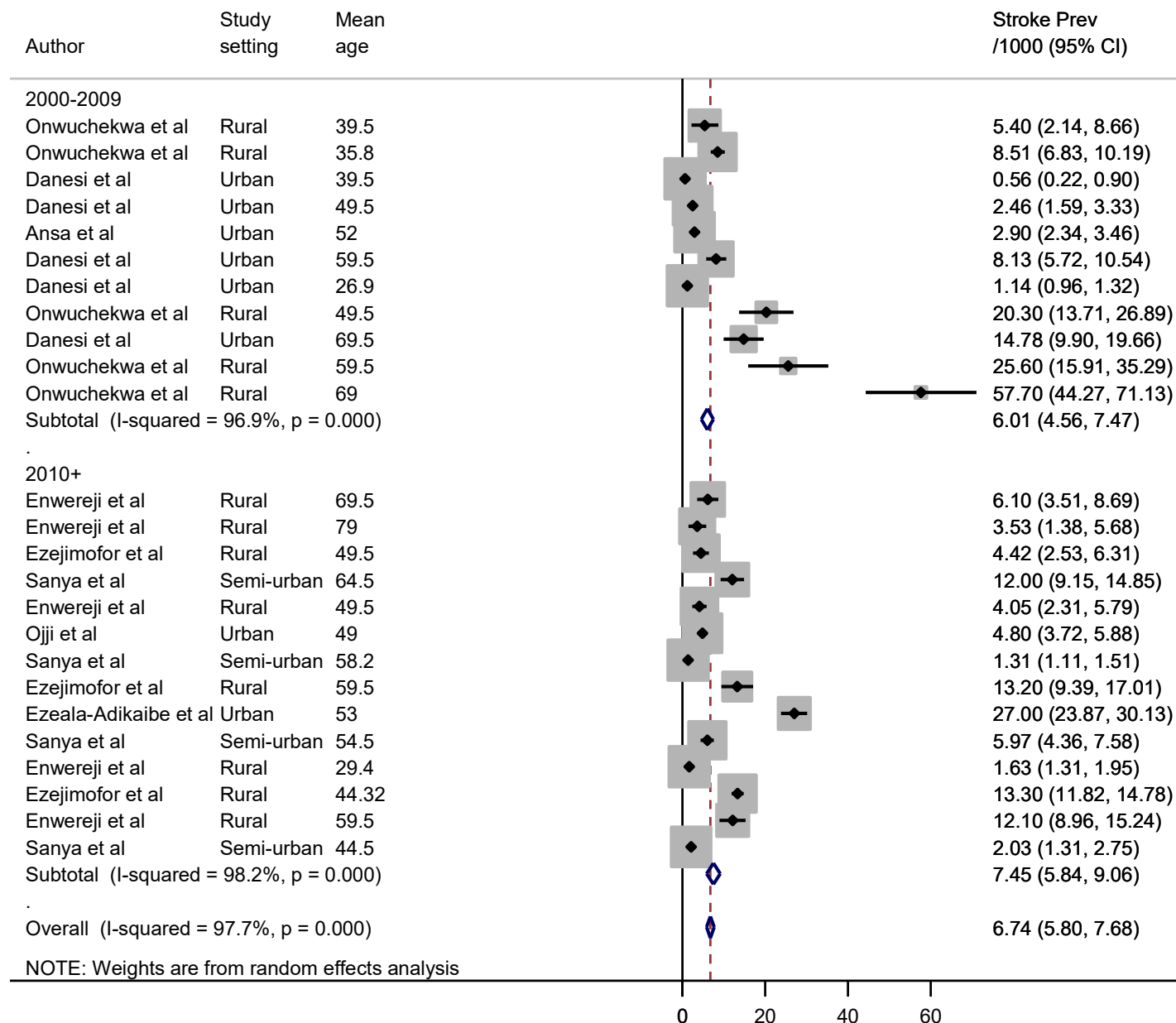


TABLE 1. Search terms on stroke in Nigeria

#	Searches
1	africa, sub-sahara/ or africa, western/ or nigeria/
2	exp vital statistics/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	case fatality rate.tw
7	hospital admissions.tw
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp stroke / or brain infarction / or cerebrovascular accident / or cerebrovascular disease / or transient ischemic attack
13	1 and 11 and 12
14	Limit 13 to "1990-current"

TABLE 2. Quality assessment of selected studies

Quality criteria	Assessment	Score	Maximum score
Sampling method (was it representative of a target subnational population?)	Yes	1	1
	No	0	
Appropriateness of statistical analysis	Yes	1	1
	No	0	
Case ascertainment (was it based on standard diagnostic criteria, other clinical criteria or case definition, informal interviews, or not reported?)	Standard diagnostic criteria	3	3
	Other clinical criteria or case definition	2	
	Informal interviews	1	
	Not-reported	0	
Total (<i>high (4-5), moderate (2-3), or low quality (0-1)</i>)			5

TABLE 3. Characteristics of studies on epidemiology of stroke in Nigeria

Author	Year	Location	Geopolitical zone	Study design	Study Setting	Quality
Adedoyin & Adesoye (20)	2001	Ile-Ife, Osun State	South-west	Hospital-based retrospective study	Semi-Urban	Moderate
Ansa et al (21)	1995	Calabar, Cross River State	South-south	Hospital-based retrospective study	Urban	Moderate
Danesi et al (22)	2007	Lagos	South-west	Population-based door-to-door survey	Urban	High
Danesi et al (23)	2006	Surulere, Lagos	South-west	Population-based door-to-door survey	Urban	High
Enwereji et al (24)	2014	Anambra State	South-east	Population-based door-to-door survey	Rural	High
Ezejimofor et al(6)	2014	Niger Delta, Delta State	South-south	Community-based cross-sectional study	Rural	High
Ojji et al (25)	2010	Abuja, FCT	North-central	Prospective cohort study	Urban	Moderate
Okon et al (26)	2011	Akure, Ondo State	South-west	Prospective cohort study	Urban	Moderate
Onwuchekwa et al (27)	2008	Kegbara-Dere, Rivers State	South-south	Community-based cross-sectional study	Rural	High
Sanya et al (28)	2010	Ilorin, Kwara State	North-central	Community-based door-to-door study	Semi-urban	Moderate
Ezeala-Adikaibe et al (29)	2016	Enugu State	South-east	Population-based cross-sectional study	Urban	High

Table 4. Pooled crude estimates of incidence and prevalence of stroke in Nigeria

Data		Both sexes		Men		Women	
		<i>Pooled rate (95% CI)</i>	<i>I², P- value</i>	<i>Pooled rate (95% CI)</i>	<i>I², P- value</i>	<i>Pooled rate (95% CI)</i>	<i>I², P- value</i>
Incidence of stroke (per 100,000 person years)	Nation-wide	25.9 (12.8- 39.0)	100, <0.001	34.1 (9.7- 58.4)	99.8, <0.001	21.1 (7.4- 35.0)	99.7, <0.001
	Study period	2000-2009	24.3 (11.9- 36.8)	100, <0.001			
		2010+	27.4 (2.2- 52.7)	100, <0.001			
	Settings	Urban	26.8 (13.0- 40.6)	100, <0.001	-	-	-
		Semi- urban	17.4 (15.2- 19.6)	-	-	-	-
		Rural	-	-	-	-	-
Prevalence of stroke survivors (per 1000 population)	Nation-wide	6.7 (5.8-7.7)	97.7, <0.001	6.4 (5.1- 7.6)	95.3, <0.001	4.4 (3.4- 5.5)	96.0, <0.001
	Study period	2000-2009	6.0 (4.6-7.5)	96.9, <0.001			
		2010+	7.5 (5.8-9.1)	98.2, <0.001			
	Settings	Urban	6.2 (4.6-7.9)	98.3, <0.001	-	-	-
		Semi- urban	4.8 ((2.5-7.1)	96.6, <0.001	-	-	-
		Rural	10.8 (7.5- 14.1)	97.5, <0.001	-	-	-
	Geo- political zones	North- central	4.8 (2.7-6.9)	96.8, <0.001	-	-	-
		South- east	8.9 (3.4-14.5)	98.4, <0.001	-	-	-
		South- south	13.4 (9.1- 17.8)	97.4, <0.001	-	-	-
		South- west	2.9 (1.7-4.1)	95.1, <0.001	-	-	-